

REMARKS

Claims 1-11 are pending in the instant applications. Claim 1-4, 6 and 7 have been rejected. Claims 1-7 have been objected to. Claims 8-11 have been cancelled as they are drawn to non-elected subject matter. After entry of these amendments, Claims 1-7 will be pending.

Objection to Claims 1-7

The Examiner has objected to Claims 1-4, 6 and 7 for containing non-elected subject matter. Applicants respectfully traverse the Examiner's objection. In Applicant's response, dated May 31, 2007, the Applicants elected Group I, which contains Claims 1-4, 6 and 7. Accordingly, Applicants respectfully request that the objection of Claims 1-4, 6 and 7 be withdrawn.

The Examiner has objected to Claim 5 for being dependent upon a rejected base claim. Applicants respectfully traverse the Examiner's objection. Claim 5 is an independent claim, therefore it is not dependent upon a rejected base claim. Accordingly, Applicants respectfully request that the objection to Claim 5 be withdrawn.

Rejection of Claims 1-4, 6 and 7 under 35 USC §112, first paragraph

The Examiner has rejected Claims 1-4, 6 and 7 under 35 U.S.C. §112, first paragraph for allegedly failing to provide an adequate written description. Specifically the Examiner stated that:

The MPEP states that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. (MPEP 2163). [F]or each claim drawn to a genus the written description requirement may be satisfied through sufficient representative number of species by (a) actual reduction to practice, (b) reduction to drawings or structural chemical formulas; (c) disclosure of relevant, identifying characteristics by functional

characteristics coupled with known or disclosed correlations between function and structure (MPEP 2163.02).

Additionally, the Examiner maintains that Applicants are claiming a large genus of compounds with substantial structural variations in Claims 1-4, 6 and 7. The disclosure is allegedly limited to a limited number of compounds reduced to practice, which is not an adequate representation of the genus claimed. The Examiner asserts that "the common structural attributes of the claimed genus, combined with a correlation between structure and function, is neither disclosed in the instant application nor commonly known in the art." To consider whether Applicants demonstrated possession of the invention, the Examiner prepared an analysis (shown below) comparing the scope of the claims and the scope of the description:

**Scope of the Claims 1-4, 6 and 7:**

R<sup>C</sup> and R<sup>C'</sup>: Independently selected from: H, (C<sub>1</sub>-C<sub>6</sub>)alkyl, aryl, heterocyclyl and (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, optionally substituted with one, two or three substituents selected from R<sup>10</sup>, or  
Optionally joined to form a monocyclic or bicyclic heterocycle comprising of one or two additional heteroatoms and optionally further substituted with one, two or three substituents from R<sup>11</sup>.

R<sup>3</sup>/R<sup>4</sup>/R<sup>8</sup>: Optionally substituted with any substituent including, for example R<sup>C</sup> and R<sup>C'</sup> and additional phosphate groups

**Scope of Disclosure**

R<sup>C</sup> and R<sup>C'</sup>: Alkyl optionally substituted with OH and tetrahydrofuran

R<sup>3</sup>/R<sup>4</sup>/R<sup>8</sup>: H or unsubstituted alkyl

Applicants respectfully traverse rejection of Claims 1-4, 6 and 7.

For a written description rejection, the Examiner has the "initial burden of presenting by a preponderance of evidence why a person skilled in the art would not recognize in an applicant's disclosure a description of the invention defined by the

claims." MPEP 2163.04 (citing *In re Wertheim*, 191 USPQ 90, 97(1976)). For Claims 1-4, 6 and 7, the Examiner has not met this initial burden of establishing a reasonable basis for questioning the Applicants completion of the written description requirement.

The Examiner states that Applicants allegedly failed to disclose common structural attributes of the claimed genus in the instant applicants. Applicants respectfully assert that all the compounds claimed in the instant application share common structural attributes, including the same 2,5-dihydro-1H-pyrrole core structure. In addition, all compounds are prodrugs of KSP inhibitors that contain a common  $-OPO(OH)_2$  group. Therefore, the genus claimed in the instant application exhibits a correlation between structure and function, which is disclosed in the instant application.

The Examiner further asserts that due to the substantial structural variation in the genus embraced by the instant claims, the number of compounds reduced to practice is not commensurate in scope with the genus claimed. The Examiner states that the core structure can be substituted with a broad array of variables, in which the variable, itself, can be optionally further substituted. For example, the Examiner claims that variables such as  $R^3$ ,  $R^4$ ,  $R^8$  can be optionally substituted with any substituent including for example... $R^C$  and  $R^{C'}$ , and that Applicants merely reduced to practice the substitution of a hydrogen atom and an unsubstituted alkyl group.

However, Applicants respectfully maintain that  $R^3$ ,  $R^4$ ,  $R^8$  can only be substituted with a substituent selected from  $R^{10}$ , which does not include the variables  $R^C$  and  $R^{C'}$ . Furthermore, Applicants maintain that at least seven embodiments of  $R^{10}$  substitutions are illustrated in the examples, schemes and/or the preferred selection sections of the specification. Representative examples are illustrated below (non-exhaustive list):

1.  $(C=O)aObC^{1-C^{10}}$  alkyl: Exemplified by Compound 4-5 (pg. 78)
2.  $CO_2H$ : Exemplified by Compound 4-4 (pg. 77)
3. halo: Exemplified by Compound 4-3 (pg. 77)
4. OH: Exemplified by Compound 3-6 (pg. 73)
5.  $O_a(C=O)_bNR^{12}R^{13}$ : Exemplified by Compound 3-6 (pg. 73)
6.  $(C=O)aObC^3-C^8$  cycloalkyl: Exemplified by Compound 3-10 (pg. 74)

7.  $-\text{OPO}(\text{OH})_2$ : Exemplified by Compound 8-3 (pg. 87)

Additionally, the Examiner claims that there is not adequate representation of the broad range of substituents defined by the variables  $\text{R}^{\text{C}}$  and  $\text{R}^{\text{C}}$ . The Examiner maintains that merely two embodiments of the  $\text{R}^{\text{C}}$  and  $\text{R}^{\text{C}}$  substituents were reduced to practice, namely an alkyl optionally substituted with a hydroxy group and tetrahydrofuran.

The Applicants respectfully assert that at least four different  $\text{R}^{\text{C}}$  and  $\text{R}^{\text{C}}$  substituents were either included as examples or disclosed as a preferred embodiment in the specification. Representative examples are illustrated below (non-exhaustive list):

1. H:  $\text{R}^1$  is an aminocarbonyl (pg. 26, line 3) -  $\text{R}^{\text{C}}/\text{R}^{\text{C}} = \text{H}$
2.  $\text{C}_1\text{-C}_6$  alkyl:  $\text{R}^1$  is an N,N-dimethylaminocarbonyl (pg. 26, line 3) -  $\text{R}^{\text{C}}/\text{R}^{\text{C}} = \text{CH}_3$
3. Heterocyclyl: Exemplified by Compound 8-4 (pg. 87) -  $\text{R}^{\text{C}}/\text{R}^{\text{C}} = \text{cyclopropyl}$
4.  $\text{R}^{\text{C}}$  and  $\text{R}^{\text{C}}$  are joined to form a monocyclic or bicyclic heterocycle:  
Exemplified by Compound 4-6 (pg. 78) -  $\text{R}^{\text{C}}/\text{R}^{\text{C}} = \text{Morpholine}$

The Applicants also maintain that adequate support exists in the specification for all of the substituents, but not limited to  $\text{R}^1$ ,  $\text{R}^{11}$ ,  $\text{R}^{12}$  and  $\text{R}^{13}$ . For example, at least five substituents for  $\text{R}^1$  are described in the specification either as a compound that has been included as an example (pg. 74, 75, 78, 79) or listed as a preferred substitution (pg. 26). Similarly, at least 3 substituents of Claim 1, variable  $\text{R}^{11}$  are included as an example (pg. 85, 89). Finally, at least 3 substituents for  $\text{R}^{12}$  and  $\text{R}^{13}$  of Claim 1 are included as an example (pg. 75, 88, 89).

According to the MPEP, the written description requirement for a claimed genus may be satisfied through a sufficient description of a representative number of species (2163.05). If the genus contains substantial variation, the Applicant must "describe a sufficient variety of species to reflect the variation within the genus" (MPEP

2163.05). Although the MPEP does not specify what constitutes a "representative number of species", typically more than one embodiment is required to satisfy the written description requirement. In the instant application, Applicants have provided a significantly more than the requisite number of embodiments to ensure that the variation within the species is reflected. In fact, the specification contains eleven generic schemes and forty-one representative examples.

Applicants maintain that the Examiner has not made a prima facie case of lack of written description, and in light of the arguments presented, it is not reasonable to conclude that Applicants have not sufficiently described the claims. Accordingly, Applicants respectfully request the rejection of Claims 1-4, 6 and 7 under 35 U.S.C. §112, first paragraph, be withdrawn.

If a telephonic communication with the Applicants' representative will advance the prosecution of the instant application, please telephone the representative indicated below. Applicants believe no additional fees are due but the Commissioner is authorized to charge any fees required in connection with this response to Merck Deposit Account No. 13-2755.

Respectfully submitted,

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